Chapter 7

APPLICATIONS OF NEAR INFRARED SPECTROSCOPY IN UROLOGY

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ABSTRACT

In biomedical and basic science applications, near infrared spectroscopy (NIRS) is an established non-invasive optical technique for measuring changes in hemoglobin concentration occurring in the microcirculation in real time. Because variations in oxygenated and deoxygenated hemoglobin and their sum total hemoglobin can be measured from baseline, graphic plots of these parameters allow changes in tissue hemodynamics and oxygenation to be inferred. This information is often not available by other means, and can contribute important physiologic insights when used alone or interpreted in parallel with other conventional measurements.

Muscle and brain have been studied using NIRS for more than 30 years. NIRS studies in the field of urology began in the 1990s, and applications to evaluate bladder hemodynamics and oxygenation are some of the most novel and recent. Such studies are relevant in a research and clinical context as bladder pathology and the voiding dysfunction that results are common, and the lower urinary tract symptoms (LUTS) that so many patients experience are problematic and negatively impact their quality of life. Various local and systemic pathologies cause bladder function to become abnormal, and NIRS has relevance as a monitoring entity as the physiologic consequences of pathology include hemodynamic problems within the detrusor microcirculation and abnormal contraction of the detrusor muscle, with ischemia and hypoxia as recognized underlying mechanisms. Urologists value the unique physiologic data NRS provides, and the non-invasive nature of NIRS is attractive to patients. Currently the principal clinical investigation used to evaluate LUTS is urodynamics (UDS); UDS measures intra-abdominal and bladder pressure as the bladder is filled through a urethral catheter, and pressure and flow as the patient voids, and so requires invasive trans-urethral and rectal
catheters. UDS is also recognized to be a limited measure in terms of the information it provides.

The rationale for using optical monitoring of the bladder is that changes in oxygenated and deoxygenated hemoglobin occur in the detrusor muscle during voiding as the organ contracts, and based on observations in NIRS muscle studies these changes will differ in health and disease. NIRS-derived parameters monitored transcutaneously in the anterior bladder wall enable variations in the organ’s hemodynamics and oxygen supply and demand to be inferred during evaluation of voiding dysfunction, which adds physiologic information that is not available from the ‘gold standard’ UDS pressure flow studies. Confidence that NIRS bladder monitoring yields physiologic data comes from the patterns of change in hemoglobin concentration observed in the bladder corresponding to changes in NIRS parameters seen in other tissues in response to known physiologic events, as does an absolute measure of tissue oxygen saturation now available during bladder studies. Hence, when interpreted based on this prior research, e.g. NIRS muscle and brain studies, bladder monitoring data are now providing novel physiologic information about the probable causal pathologies that underlie voiding dysfunction.

The feasibility of other applications of NIRS in urology have been demonstrated, including measures of renal function, hemodynamic monitoring of the testis, and evaluation of the pelvic floor in women. A range of studies have been conducted in both genders that have included children as well as adults.

The NIRS instruments used in urology have evolved from bench-top laser powered systems to self-contained miniaturized devices incorporating light emitting diodes, spatially resolved optical geometry, and wireless capacity. These advances make more advanced yet lower cost devices available that open new avenues for NIRS monitoring in ambulant subjects, and in special populations such as children and patients requiring long-term monitoring.

Biomedical applications of NIRS in urology represent a ‘disruptive’ technological advance of relevance as they provide a non-invasive, portable, real time measure of changes in bladder perfusion and oxygenation. Hence NIRS monitoring offers an opportunity to add new knowledge regarding the physiology of the bladder, the pathologies underlying voiding dysfunction, and the potential effectiveness of therapeutic agents. Studies to date warrant further research, continued refinement of NIRS instrumentation, and exploration of the role of diagnostic software algorithms.

**Keywords:** bladder, kidney, near infrared spectroscopy (NIRS), penis, testis, urology, urinary tract, urinary incontinence

**INTRODUCTION**

Biomedical applications of near infrared spectroscopy (NIRS) use energy from light in the near-infrared (NIR) spectrum to monitor changes in local blood volume and detect differences in tissue oxygen delivery, consumption, and utilization [1-4]. NIRS monitoring shares many technical principles with pulse oximetry, and has been widely applied as a research tool [5,6]; there are comprehensive reviews of the applicable science, instrumentation, methods of measurement, and limitations, and applications for clinical monitoring [1,2,5,7-10]. Recent studies have used NIRS to investigate urologic conditions, and now NIRS bladder monitoring offers urologists additional physiologic information of relevance for evaluation of patients with voiding dysfunction [11,12].
NIRS Principles Central to Studies in Urology

At most wavelengths of the light spectrum, light is absorbed by skin and tissue, but photons of light generated in the near infrared (NIR) spectrum, 700-1300 nanometers (nm), pass through skin, sub-cutaneous tissue and bone, and scatter in tissue [5]. Naturally occurring compounds (chromophores) absorb these photons in varying amounts depending on the chemical structure, color, and concentration of each chromophore, and the wavelength of the light transmitted. It is the unique relationship between the transparency of tissue to NIR light and the specific absorption spectra of individual chromophores that provides the basis for clinical studies using near infrared spectroscopy [1,5,6].

The principal chromophore of interest in biomedical studies is hemoglobin which has a different extinction coefficient (absorption characteristic) across the NIR spectrum when oxygenated (O₂Hb) and deoxygenated (HHb) [13]. Water is also a chromophore of relevance in urologic studies, and there is the potential to monitor change in concentration of cytochrome-c-oxidase (CCO) which also absorbs light differently across the NIR spectrum depending on its redox status; the relevance of CCO is that it is the terminal enzyme of the mitochondrial respiratory chain [14,15].

In the majority of urological studies to date continuous wave (CW) instruments have been used with lasers that transmit multiple wavelengths of light into tissue [11,16]. Sensors (photo multipliers or photodiodes) detect the photons returning that are neither scattered nor absorbed by chromophores. The depth of penetration of NIR photons into tissue is a factor of the distance between the emitter and detector, or inter-optode distance (IOD) [17,18]. Figure 1 illustrates a NIRS system configured for transcutaneous monitoring of the bladder, and the ‘banana’ shaped field of view generated with the emitter and detector in reflectance mode by the penetration of NIRS photons into human tissue.

Figure 1. Schematic diagram showing the set up for wireless NIRS monitoring of the bladder.
Software algorithms convert the raw optical data into concentration changes for each chromophore from baseline using a modification of the Lambert-Beer law [5,19]. These algorithms also accommodate for a number of limitations posed by the nature of human tissue, including where the path length of NIR light and number of photons lost due to scattering are unknown [6].

NIRS can only measure absolute changes in concentration relative to the initial baseline concentration because the full extent of the field through which NIR light scatters is always unknown in vivo. However, with real time sampling and graphic conversion of data, patterns of change in chromophore concentration and magnitudes of change are derived which can be used to infer physiologic change occurring within the tissue interrogated [1,7,10]. Such changes include: an increase or decrease in $O_2$Hb (an indirect measure of oxygen content); an increase or decrease in the sum of $O_2$Hb and HHb, total hemoglobin (tHb) (a change in blood volume); a gradual decrease in $O_2$Hb and matching increase in HHb (hypoxia); and an abrupt decrease in $O_2$Hb with simultaneous fall in tHb and increase in HHb (ischemia).

Monitoring the redox status of cytochrome-c-oxidase (CCO) potentially provides information relating to electron transport and oxidative phosphorylation at a cellular level, as CCO drives $> 95\%$ of $O_2$ consumption and the synthesis of adenosine triphosphate (ATP) within mitochondria [6,15]. The bladder mitochondria contain significant quantities of CCO, however, only one preliminary study on cytochrome redox status has been done to date [20]. This aspect of NIRS monitoring has been investigated principally in the brain and spinal cord in animal models and human studies [21-23]; the technical challenge is that the contribution of CCO to overall absorption of NIR light during NIRS monitoring is considerably smaller than that of hemoglobin (approximately one tenth) [14].

**Instrumentation**

Laser powered continuous wave (CW) NIRS instruments were used for the first applications in urology and typically incorporate the following [11,24]:

- a) At least one pulsed laser diode for each chromophore being sampled. Typically the lasers emit light in 1, 2 or 4 wavelengths in the 729 to 920 nm NIR wavelength range with a 5 nm spectral width and pulse duration of 100 nanoseconds at 2 kHz cycle frequency;
- b) Fiber optic bundles that transmit light from the source to a tissue interface (probe or patch) and back to the instrument;
- c) Optodes in the tissue interface that emit light into the tissue and receive the photons returning;
- d) Photon counting hardware (photomultiplier or photodiode);
- e) Computer with software containing algorithms for converting raw optical data into chromophore concentrations, storing and displaying data;
- f) A visual display where NIRS data are typically displayed graphically against time.

Lasers provide high spectral resolution and high sensitivity with ultra-fast photo detectors, [5,11] but the instruments tend to be large and the patient is constrained during monitoring by the fiber optic cables required to carry light between the instrument and the
emitter/detector patch on the skin. Some instruments provide a choice from multiple wavelengths, and the option to use more than one data channel to allow comparison of different sites is available. This ability was used to confirm that signals occurring during voiding were only detected over the bladder not from a control channel on the upper abdomen [25,26]. Some multiple channel instruments have the capacity for functional monitoring (fNIRS) using an array of multiple emitters and receivers, with data displayed in the form of a regional map or real time video of hemodynamic change [27,28].

Light emitting diodes (LEDs) are an alternative NIR light source to lasers. LEDs have minimal power consumption so can be powered by small batteries, and because the light source is non-coherent and non-collimated can provide high light intensity levels. [11,16,29] Very small self-contained wireless NIRS devices have been designed that make use of LEDs, and such devices enable subjects to be monitored more simply than with laser powered instruments requiring fiber-optic cables. Such devices now make it possible to monitor subjects undertaking a growing range of active physical pursuits, to study small children, and to monitor ambulant patients over time. However, in the context of design, elements of compromise are required when choosing the LEDs, detectors, batteries, and telemetric communication components in particular for wireless systems. For example ‘Bluetooth’ capacity while ideal for potential linkage to remote data storage modules, and especially mobile phones, does use more power than other wireless communication systems, which results in the need to incorporate a battery with higher capacity.

An important innovation is that LED wireless devices can now be configured with the optical geometry required for spatially resolved spectroscopy (SRS) which enables an absolute measure of tissue oxygen saturation to be obtained. SRS requires two or more emitters positioned at different distances from the detector to allow measurement of intensity as a function of distance; with appropriate algorithms the ratio of oxygenated to total tissue hemoglobin is then calculated from which an absolute measurement of tissue oxygen saturation can be made [30-32]. Tissue oxygen saturation values predominantly reflect venous oxygen saturation as only the minority of the blood in tissue is in capillaries and arterioles; and in SRS the assumption is made that the tissue interrogated is homogenous. The terms used for the measure of oxygen saturation obtained differ depending on the manufacturer of the device. The values derived are also not directly comparable between devices due to a number of key differences including variations in the software algorithms employed [6]; but measurements can be made in real time and are of recognized value. CW SRS NIR instruments of small size and with telemetric capacity represent an important advance in the application of NIRS in both a research and clinical context, and are the wireless devices most recently used in urology to monitor changes in bladder hemodynamics, oxygen supply and demand, and measure tissue oxygen saturation in the detrusor muscle [11,16,30,33,34].

The commercially available wireless device most widely used is the ‘Portamon’ (Artinis Medical Systems BV, The Netherlands) [11,16] Figure 3. It is also the instrument our group is most familiar with from experience gained in studies monitoring voluntary muscle oxygenation and hemodynamics during exercise, surgery, and induced ischemia [33-38], and physiologic changes in the detrusor muscle of the urinary bladder during the voiding cycle. The ‘Portamon’ measures 83 X 52 X 20 mm, weighs 84 gm, and uses paired light emitting diodes with wavelengths of 760 and 850 nm as the NIR light source. Three pairs of these LEDs are mounted in configuration for SRS with the single detector providing 3 source-detector separation distances (30, 35 and 40 mm). The detector is a silicon photodiode with a
filter to provide ambient light protection. Data is collected at 10 Hz. Power is supplied by a rechargeable Lithium Polymer battery with the capacity for about six hours of continuous monitoring. The unit has a 2 megabyte internal memory to store data during ambulatory measurement, and incorporates ‘Bluetooth’ technology with broadcast range of 20 meters to transfer data to a laptop computer for data analysis, graphic display and storage. The instrument is attached to a subject by means of an adjustable strap or tape.

Figure 2. The wireless device (‘Portamon’) positioned on the lower abdomen for NIRS bladder studies in a child. Inset shows the configuration of the 3 paired LED emitters and single photodiode detector.

Proprietary software (‘Oxysoft’, Artinis Medical Systems BV, The Netherlands) [26] allows data interpretation at each source-detector distance, and derives changes in the concentration of the chromophores \( \text{O}_2\text{Hb} \) and HHb from the raw optical data, total hemoglobin (tHb) as the sum of \( \text{O}_2\text{Hb} \) and HHb, and an absolute measure of tissue oxygenation (expressed as tissue saturation index or TSI %). There is also an option for an in built accelerometer. Applications in addition to those in urology include sports science, athletic training evaluation, rehabilitation medicine, high altitude research, orthopedics, occupational health, and peripheral vascular disease [16].

As with NIRS research in other fields it is important when reporting urologic studies that the characteristics and limitations of the hardware, and software algorithms of the NIRS equipment employed are described, as these elements each impact the data obtained. In urology, as elsewhere, NIRS hardware and software are continuously evolving.

**BLADDER ANATOMY AND PHYSIOLOGY RELEVANT TO NIRS STUDIES**

Transcutaneous CW NIRS is an ideal monitoring technology for the bladder because real time changes in hemodynamics and oxygenation can be detected as the bladder fills and empties [11,12,16,30,34,39,40]; and the bladder is an ideal organ for NIRS because of the nature of its blood supply and anatomic location in the lower abdomen [41,42]. Importantly,
recognized confounders for NIRS monitoring are also minimal in number; there are not multiple layers of tissue/bone/fluid with different attenuating properties between the emitter/detector and the tissue of interest. Even fat is relatively sparse in the lower abdomen at the site used for optimal interrogation of the bladder – 2cm superior to the pubis. Fat absorbs approximately 5% of NIRS photons in ‘lean’ tissue, but the NIRS signal is blunted significantly when substantial subcutaneous fat is present because of the optical characteristics and oxygen consumption of adipose tissue [43,44].

Anatomy

The anatomy and location of the bladder and how its dimensions alter as it fills and empties are relevant to NIRS monitoring. The base of the bladder is attached within the pelvis which dictates the consistency of the organ's position [42]. Stothers et al. [41] reported ultrasound data from 28 women showing the mean depth of the anterior wall of the bladder below the abdominal skin was 2.7 cm (range 1.24-3.95); also that the anterior wall retains its position in relation to the abdominal wall as the organ fills and empties. These data also show that mean thickness of the abdominal fat layer below the site for the emitter/detector is also favorable to NIRS monitoring (in the order of 8 mm).

Vasculature

The vascular structure of the bladder is uniquely configured to enable the organ to be both distensible for storage and contractile for voiding, and yet provide the detrusor muscle in the bladder wall with the oxygen and nutrients required for normal function when the organ is healthy [42,45,46]. However, the integrity of the bladder’s microcirculation is recognized to be compromised by multiple pathologies associated with bladder dysfunction and by aging [47-54], and NIRS research to date indicates that patterns of chromophore change in the anterior bladder wall as the organ fills and empties have important differences in health and disease.

For normal storage and contractile function the bladder must be adequately perfused. The urinary bladder is a richly vascularized organ [42,55], and it is the unique architecture of the vessels in the organ’s microcirculation that makes consistent perfusion possible by accommodating for the major spatial changes that occur as the organ fills and empties [45,46]. These changes involve the bladder wall stretching and thinning during filling and contracting and thickening during voiding – mechanical changes capable of compromising blood flow in the absence of an adaptive microcirculation.

Within the layers of the bladder wall there are two major vascular plexuses (adventitial/serosal, and mucosal), and two distinct capillary networks (muscularis, and subepithelial) [56]. The adventitial/serosal plexus is formed by large branches of the main vesical arteries and veins; these vessels have a highly tortuous course and numerous anastomoses. The mucosal plexus consists of capillaries, thin arteries (50–100 μm in diameter), and more numerous thicker veins (80–250 μm). These vessels are again tortuous with frequent interlacements, and form a distinct vascular layer parallel to the inner surface of the bladder which follows the profile of the mucosal folds [57]. The muscularis capillary
network consists of thin uniform vessels (8–12 μm), with occasional very tortuous arterial and venous branches mostly derived from the adventitial/serosal plexus. The principal vessels are distributed in flat sheets probably corresponding to the connective tissue septa between the smooth muscle bundles in the bladder wall. In contrast, the subepithelial capillaries form an extremely dense planar network and have larger diameters (10–20 μm) or uneven contours with constrictions and dilatations.

**Contractile Properties**

During urination bladder contraction is dependent on the integrity and function of the detrusor muscle (muscularis propria). The detrusor contracts over a large length interval during urination but at other times remains relaxed which allows the bladder to fill [52,58]. The detrusor is made up of smooth muscle fibers arranged in spiral, longitudinal and circular bundles in the bladder wall below the mucosal folds that line the lumen, and in close proximity to arterioles and venules. The detrusor is stimulated to contract by parasympathetic nerve signals generated as the bladder wall is stretched [59]. Muscles envelop the urethra (urethral sphincter muscles) which also control the flow of urine when they contract, and the sphincter is another area with a rich neurovascular network. Sphincter function is an integral factor in normal bladder filling, retention of urine, and voiding especially in females [60].

**Normal Bladder Function**

In healthy humans the microvasculature maintains tissue oxygenation as metabolic demands change via neuronal, endothelial and erythrocyte mediated signaling pathways that integrate smooth muscle and endothelial cell function, determine convection and diffusion of oxygen, and dictate where blood flow is distributed [61-63]. In the bladder it is presumed that similar mechanisms provide for adequate perfusion, for normal bladder filling, urinary retention, and voiding to occur, including during the increased metabolic demand of contraction of the detrusor and urinary sphincter muscles. Blood vessels present in the bladder submucosa must have extreme flexibility as this tissue undergoes the most extensive deformations as the bladder fills and empties. During normal filling and expansion of the bladder, the organ’s microvasculature undergoes topographical rearrangement with straightening and stretching of the vessels. This scenario results in decreased resistance and increased blood flow despite a likely increase in bladder wall tension. Then, as the bladder approaches its maximum capacity the intravesical pressure increases, and the microvasculature within the thinning bladder wall is likely compressed. The cells lining the lumen of the bladder (urothelium) also have an integral role in voiding function; releasing chemicals that alter the excitability of afferent nerves and initiating mechanosensory transduction via reciprocal interactions with afferent and efferent nerves [59].

Kershen et al [46] have shown that during the filling phase bladder blood flow increases approximately 1.8 times over that of the empty bladder, then as the volume of urine approaches 100% of maximum bladder capacity intravesical pressure increases more rapidly, and bladder blood flow decreases significantly to about 1.2 times that of the empty bladder. However, because of the increase in blood flow associated with filling, it remains above basal
blood flow in the empty state despite the increase in intravesical pressure. Immediately after the bladder empties a rebound increase in flow occurs, raising blood flow to about 1.6 times that of the empty bladder.

The tortuosity of blood vessels in the muscularis and in the outer adventitial/serosal plexus helps to accommodate stretching of the smooth muscle layers, and the increase in the outer perimeter of the bladder. The long perpendicular vessels that pass through both muscularis and submucosa most probably adapt to the altering thickness of the bladder wall via a coiling/uncoiling mechanism [45].

Normal bladder function also requires neural pathways to be intact between the bladder and the areas of the brain involved in bladder sensation and control [52,59]. Normal voiding involves a spino-bulbo-spinal reflex mediated by the brain while urine storage is dependent on lumbosacral spinal reflexes. Griffiths et al have used functional MRI to identify the brain regions involved in voiding and bladder control, and their response to a variety of bladder sensations [64,65]; fNIRS can also be used to detect cortical brain activity, but is probably not the optimal way to study the relationship of these regions to bladder responses during voiding due to the location and particularly the depth of the centers involved.

Impaired Storage and Voiding

Voiding dysfunction is a significant health burden as population’s age [66,67]. Hence the relevance of exploring effective alternatives to invasive diagnostic studies, such as NIRS. A range of symptoms involving the lower urinary tract are indicative of impairment of detrusor function. One mechanism underlying voiding dysfunction is where bladder blood flow and perfusion are abnormal; this situation can result from a number of systemic and local pathologies. We hypothesize that the common pathway for such pathologies is an adverse effect on the hemodynamics of the detrusor microvasculature, that compromises the increase in the provision of oxygenated blood required for normal detrusor contraction and/or results in an imbalance in oxygen supply and demand as voiding occurs. It is possible that dysfunction of the endothelium of the microvasculature is the primary mechanism for this effect as the normal healthy endothelium regulates vascular tone by the release of numerous dilator and constrictor substances [68] Nitric oxide (NO) is the principal endogenous vasodilator; NO opposes endothelium-derived vasoconstrictors; damage to the endothelium upsets the balance between vasoconstriction and vasodilation; the hallmark of endothelial dysfunction is impaired endothelium-dependent vasodilation [69]. A defect in NO production or activity manifested as impaired vasodilation has been suggested as one of the earliest signs of peripheral vascular disease, and endothelial function is known to be adversely affected by pathologies such as hypertension, hypercholesterolemia, and diabetes, and the effects of cigarette smoking [69-71].

A variety of changes in the pattern of chromophore change observed in dysfunctional voiding have been observed; these match patterns seen in other tissues in response to hemodynamic change and disordered oxygen supply and demand, and at their most extreme even imply that interruption of detrusor blood supply can occur that results in bladder ischemia, ultimately followed by reperfusion [45,53]. Experimental studies reveal that chronic bladder ischemia is associated with marked changes in detrusor compliance and
contractility [53]. Detrusor instability, loss of bladder compliance, and structural changes in the human detrusor also occur with aging [54].

APPLICATIONS IN UROLOGY

Urologic conditions studied using NIRS include testicular ischemic conditions, erectile dysfunction, and renal dysfunction. In addition, NIRS has been used to study skeletal muscle metabolism in patients with end stage renal disease, and the toxic effects of contrast media. Most recently the bladder, urinary sphincter, and pelvic floor have been studied to establish the NIRS changes observed during normal voiding, and the effects of a variety of pathologies that cause voiding dysfunction in both genders, and in adults and children.

Initial Applications

The first application was reported by Colier et al. in 1995 [72], who used NIRS in combination with pulse oximetry to measure the blood supply to intra-abdominal testes in an animal model of cryptorchidism. They hypothesized that NIRS combined with pulse oximetry would provide measurement of blood flow to the testis as a whole, and allow calculation of the active testicular blood volume before and after temporary occlusion of the spermatic vessels. The technique was performed in 10 boars with either normal or intra-abdominal testis, and demonstrated that with intra-abdominal testis, because of subsequent atrophy, there is no significant active testicular blood volume after temporary ligation of the spermatic vessels. They proposed that NIRS combined with pulse oximetry could quantify changes in testicular blood volume in real time, which in turn could be used as a measure of the viability of an abdominal testis.

Caprarro et al [73] also used NIRS to monitor testicular blood flow and assessed the feasibility of detecting acute testicular hypoxia in a sheep model of testicular torsion. They hypothesized that NIRS would offer an effective means of evaluating testicular blood circulation, recognizing that blood flow in a symptomatic testis is decreased or absent, and the importance of early and accurate diagnosis. The study showed sensitive detection via NIRS of testicular hypoxia following testicular torsion and also reperfusion of the hypoxic testis after torsion was reduced. Frequency domain NIRS studies have been reported in rabbits [74], and comparison in the rat model of NIRS-derived absolute oxygenation measurements with Doppler ultrasound data, coupled with immunohistochemical diagnostic confirmation of testicular ischemia [75]. Bergu et al then recently described a pilot study in adult humans [76] where an absolute measure of testicular tissue oxygen saturation was used to compare the vascular status of the right and left testes in suspected torsion. In the 11 patients confirmed by surgical exploration to have testicular torsion, trans-scrotal NIRS of the affected testis showed significantly reduced oxygenation at presentation, and improvement following detorsion. Technology such as Doppler flow studies has limited applicability as a diagnostic measure, is less easy to use than NIRS, and requires a radiologist [76], making further exploration of the use of NIRS logical because of the proven ability of the technology to detect impaired oxygenation due to ischemia in real time.
Burnett et al [77] used NIRS to study the physiology and vascular properties of the penis related to erection. Despite awareness that hemodynamic variables underlie vasculogenic erectile dysfunction, and development of a wide range of study methods, there is still no single “gold standard” test for diagnosing this condition [78]. Penile spectroscopy was performed on 38 patients with erectile dysfunction and 18 volunteer subjects using a customized NIRS probe with wavelength of 805 nm with simultaneous color duplex ultrasonography, strain gauge penile circumference monitoring, and penile tonometry. Penile blood volume changes and their time course were documented following intracavernous stimulation. The conclusion was that NIRS can evaluate hemodynamic phenomena in the penis and discerns erectile end-organ failure. NIRS was suggested as a method of producing diagnostic ranges that identify non-vasculogenic to severe vasculogenic causes of erectile dysfunction, with the aim of helping urologists to predict which patients would most likely benefit from first-line pharmacological treatments.

Petrova and Mehta [79] studied 10 mechanically ventilated preterm neonates (24-32 weeks gestation) to evaluate the effect of hypoxic episodes on cerebral and renal tissue oxygenation. Prior studies using simultaneous NIRS and pulse oximetry had shown a direct correlation between arterial oxygen saturation and cerebral tissue oxygenation [25], and as isolated hypoxic episodes occur frequently in preterm neonates the effects of such episodes on the brain and kidney are relevant. Arterial oxygen saturation by pulse oximeter and cerebral and renal venous oxygen saturation via NIRS were monitored simultaneously with NIRS transmitter/receiver patches placed on the forehead and on the skin of the thoracolumbar region over the right kidney. During 20 episodes of decreased oxygen saturation (SaO₂ < 80% for > 4 seconds) fractional oxygen extraction in cerebral tissue was comparable to non-hypoxic controls, but increased oxygen extraction occurred in renal tissue. Obvious advantages of using NIRS in this study were its non-invasive nature, the ability to study infants at the bedside without the need to move them from the nursery, the safety of light as an energy source, and continuous data collection over time.

Three studies addressed aspects of renal failure. Vaux et al [80] studied the effect of L-carnitine supplementation on muscle bioenergetics in patients with chronic renal failure (CRF) on hemodialysis. Hemodialysis (HD) patients have skeletal muscle wasting and impaired exercise tolerance due to reduced oxidative capacity, and also become carnitine deficient. MRI and NIRS studies were done on calf muscle in 13 patients with CRF on maintenance hemodialysis 2-3 weeks before and 16 weeks after administration of L-carnitine. NIRS was used to monitor oxygenated hemoglobin, deoxygenated hemoglobin and myoglobin concentration before and after an exercise protocol. The measures used were the half-time for recovery of the NIRS signal as an indicator of tissue oxygenation and return of perfusion to resting level after exercise. No significant effects of L-carnitine on objective measures of muscle metabolism, function and bioenergetics or any clinical improvement was found. Kemp et al [81] evaluated the contributions to skeletal muscle dysfunction of reduced muscle section area, intrinsic mitochondrial dysfunction, abnormal contractile efficiency and reduced muscle oxygen supply in similar patients with CRF on HD. Calf muscle was studied with NIRS in 23 HD patients and 15 control subjects at rest, and during and after an exercise protocol, and muscle oxygenation and perfusion compared. It was concluded that muscle dysfunction in HD patients is related to a mitochondrial defect. Matsumoto et al. [82] measured skeletal muscle oxidative metabolism in children with end stage renal disease. NIRS was performed on the forearm in 10 patients before and after renal transplantation, and
alterations in Hb/Mb (myoglobin) deoxygenation during arterial occlusion compared as an indicator of the rate of oxygen consumption in mitochondria, and recovery time as an indicator of muscle aerobic capacity following a hand-grip exercise. Oxidative metabolism in skeletal muscle during exercise was impaired and improved remarkably after renal transplantation.

Krause et al [83] used NIRS in an animal model to assess renal tolerance to contrast agents with differing osmolality and study the effects of addition of a prostacyclin analogue. A small NIRS probe was placed on the renal cortex of rats to measure alteration of tissue oxygen saturation after injection of iodinated contrast media, and after addition of iloprost. A significant decrease in total hemoglobin, oxygenated hemoglobin and tissue oxygen saturation occurred in the kidney after injection of contrast media, and iloprost attenuated the decrease in oxygen saturation. Contrast agents have a direct effect on glomerular filtration and medullary blood flow; development of less toxic contrast media has long been a subject of research in uroradiology [84].

In brain studies related to voiding Matsumoto et al [85] used fNIRS to monitor changes in the relative concentration of O$_2$Hb as a measure of variations in frontal lobe blood flow over cortical brain areas involved in the control of micturition. Studies using a 52 channel NIRS machine compared such changes before and after voiding, and during compression of the lower abdomen to simulate the urge to void in 20 control subjects. Sakibara et al [86] also reported fNIRS studies comparing normal controls with subjects with detrusor over activity (DO). A continuous increase in O$_2$Hb concentration was evident in the frontal micturition areas in 5 adult controls during natural bladder filling to the point. Just after voiding began, while a continuous decrease occurred after voiding. In contrast, in 4 subjects with DO it was rare to see an increase in O$_2$Hb before the first sensation to void occurred, and frontal cortical activation was weak.

**Other Spectroscopic Techniques Applied in Urology**

Spectroscopic techniques other than continuous wave NIRS have been used to evaluate the genitourinary system. [6,25]. These techniques vary from CW NIRS in how they apply the physical principles of absorption, emission and scattering of different wavelengths of light. NIRS (absorption spectroscopy) measures light absorbed [87]. Fluorescence (reflection) spectroscopy (FS) measures the amount of light reflected from a substance to detect differences in the fluorescent properties of pathologic tissues [88]. This technique relies on differences in fluorescent emission of photons by different molecules when they are exposed to a monochromatic light source such as a laser. Raman (scattering) spectroscopy, measures the wavelengths that a substance or tissue reflects upon excitation by laser light and generates unique Raman spectra in vitro that can be used to determine the composition of the tested sample [89]. Time resolved (TR) spectroscopy measures the time of flight in addition to light intensity and is used experimentally to determine the optical properties of tissues, three-dimensional imaging, and tomography [6,13].

FS has been used to explore differentiation of normal from neoplastic epithelium, including differentiating normal urothelium from transitional cell carcinoma of the bladder. Although several reports have confirmed the high sensitivity of this technique the specificity is low.
RS provides detailed cellular analysis and an objective method for diagnosis of pathology such as cancer and infection, and in urology shows promise for in vitro diagnosis and grading of bladder and prostate cancers. RS can also be used to identify the composition of urinary stones and their effect on renal medullary collecting ducts through analysis of biopsies from renal papillae. New developments in RS will likely provide in vivo urological applications for guiding endoscopic procedures and assessing tumor resection margins. Other extensions of spectroscopic technology such as TR are being explored experimentally to examine the optical properties of prostatic tissue in vivo in the context of developing photodynamic therapy as a modality for the treatment of prostate cancer.

Amelink et al. [90] have demonstrated the feasibility of using differential path length spectroscopy (DPS) to measure microvascular oxygenation in the human bladder. The technique involved is invasive, but measurements are possible on both the inside and outside surfaces of the bladder wall. In future this DPS technique and other spectroscopic technologies could be used in conjunction with transcutaneous NIRS to learn more about the microcirculation of the bladder; especially to determine whether disease affects both the muscle and the urothelial vasculature, or if it is principally limited to the more complex urothelial system.

**NIRS Monitoring of the Bladder**

Our group first reported the feasibility of using NIRS in the evaluation of bladder function. Macnab et al described simultaneous trans-abdominal NIRS of the bladder during urodynamic evaluation of an adult patient with urinary incontinence [91] and demonstrated a temporal change between $O_2$Hb and HHb concentration during voiding. Subsequent studies have explored the potential of non-invasive transcutaneous NIRS to study bladder filling and emptying in normal subjects, and distinguish between specific urinary pathologies using the patterns of chromophore change generated by NIRS monitoring during simultaneous urodynamic studies. Most recently absolute changes in detrusor oxygen saturation have also been compared in health and disease measured via a tissue saturation index (TSI %) using a wireless NIRS device with spatially resolved optical geometry.

**The relevance of NIRS for bladder monitoring.** Bladder disease and related problems with urination constitute a major health problem [66,67]. Over one million new patients present for evaluation annually in the USA alone, and worldwide numbers are increasing amongst ageing populations, although no age group is immune [92]. Problematically the current ‘gold standard’ method for evaluation of bladder dysfunction, urodynamic pressure flow studies (UDS), is recognized to have limitations. This test only provides values for the pressure within the bladder and rate and volume of urine flow, and generates little direct information about the causal pathology underlying the voiding dysfunction. UDS testing involves a number of elements (Figure 3) and is an invasive procedure that requires placement of catheters into the bladder and rectum for measurement [93-95]. Having a catheter in the urethra compromises the physics of flow and hence measurement; there are significant health risks associated with catheterization; and the invasive nature of this investigation makes many patients decline to have it done.
Study technique: A methodology report [40] describes how to conduct simultaneous NIRS monitoring of detrusor hemodynamics and oxygenation during UDS pressure flow studies. NIRS data are collected via a patient interface placed on the abdominal skin over the anterior wall of the bladder 2 cm above the symphysis pubis and across the midline. With the first laser powered instruments the interface contained an emitter and detector housed in an adhesive patch and was connected to the device by a fiber optic cable [24]; and with current self-contained wireless devices the same site on the abdomen is used but the whole device is located in this position, with the light emitters and photodiode detector placed across the midline over the anterior wall of the bladder [33]. It was determined that a 4 cm separation between the emitter and detector enabled the detrusor to be interrogated in all but the most obese subjects. With the current wireless device three different separations are provided by the spatially resolved optical geometry configured for measurement of absolute tissue oxygen saturation [11,16]; the incorporated software also allows chromophore data to be analyzed at three different depths of penetration.

NIRS monitoring can be done during free uroflowmetry or simultaneously during invasive cystometry and pressure flow studies (UDS). [40] Events are recorded in the data stream, as are bladder sensations related to urge, urgency and capacity. A unique feature of NIRS is the ability to collect data during natural filling and voiding without the presence of a catheter. Also NIRS data changes are evident following the command ‘permission to void’ and prior to the point that urine flow begins; a time interval when invasive UDS tracings are ‘silent’ as no flow has begun, but where significant physiologic events related to the initiation of voiding are taking place [11,34]. Presumably the changes in bladder hemodynamics
observed during this period represent brain mediated effects related to the initiation of voiding.

NIRS monitoring during natural filling and voiding involves the following steps:

1. The subject allows his/her bladder to fill naturally; water may be drunk ad libitum during this time.
2. Ultrasound of the bladder to determine the organ’s size and urine volume. (Optional)
3. Attach NIRS emitter/detector patch or wireless device to the abdominal skin with the emitter and detector(s) across the midline 2 cm superior to the symphysis pubis.
4. Begin data collection; or baseline data for 30 seconds; subject remains still.
5. Instruction given to empty the bladder “permission to void” and event marked in the data stream.
6. Subject spontaneously voids into a uroflow meter, and events marked for start and end of voiding.
7. Post uroflow data collection for one minute, then pause NIRS data collection.
8. Record volume of urine voided.
9. Remove NIRS emitter/detector patch or wireless device.
10. Ultrasound measurement of post voiding residual urine volume (PVR) in the bladder. (Optional)

*Patient selection:* Asymptomatic subjects and patients of both genders with a broad range of symptoms have been included; the age range in these studies was from 5 - 78 years. In practice almost all patients with voiding dysfunction can be monitored because of the optical nature of the technology, and NIRS monitoring is readily accepted by patients because of its non-invasive nature. High Body mass Index (BMI) is a potential limiting factor as NIR light penetration is influenced by body fat. A BMI in excess of 30 kg/m² has been identified to preclude measurement, and hematuria is a contraindication to NIRS monitoring as the absorption of light by hemoglobin in the urine is a potential confounder.

*Data display:* NIRS data can be displayed in a number of ways. Device software usually provides for graphic display of changes in concentration of individual chromophores and their sum total hemoglobin against time. Although convention varies the colors for display are usually red for O₂Hb, blue for HHb, and green for tHb. With simultaneous UDS testing NIRS parameters can be included and synchronized with UDS data graphics and events; this is important for interrelating UDS and NIRS data, but the resulting composite graphs are complex (see example in Figure 6). We find the NIRS data trends and relationships easier to interpret if we also overlay the O₂Hb, HHb, and tHb plots, and usually bias the data at a specific point (e.g. permission to void); this eases interpretation of events over the voiding cycle and comparison between studies (see example in Figure 4). Care must be taken on composite graphs to have a sufficiently large scale for changes in chromophore concentration to be visible; tracings can also be filtered to smooth the graphics generated.

*Asymptomatic (normal) subjects:* In asymptomatic children and adults during natural voiding a positive trend in tHb is usually seen following permission to void that predominantly reflects a rise in O₂Hb. A further increase in blood volume/oxygenated hemoglobin supply then usually occurs as the flow of urine begins, and the HHb concentration is essentially unaltered between the start and end of urine flow indicating a
balance of oxygen supply and demand during voiding [11,34,96]. This pattern of change is illustrated in Figure 4.

Figure 4. Chromophore patterns of change during voiding in an asymptomatic 7 year old girl. The changes in concentration are overlaid and biased to zero at the time point when permission to void was given.


Figure 5. A composite graph of UDS and NIRS parameters in a 64 year old man with LUTS associated with BOO. Following permission to void (P) an increase in total hemoglobin (tHb) occurs due to a rise in oxygenated hemoglobin (O$_2$Hb). Following uroflow start (S) a marked decrease in O$_2$Hb occurs reflected by a comparable fall in tHb; this trend is evident up to the point of peak urine flow (Qmax), and towards the end of voiding (E) O$_2$Hb rises with a corresponding increase in tHb. This implies a decrease in the provision of oxygenated blood to the detrusor during the first two thirds of the voiding cycle.
**Bladder outlet obstruction:** Macnab and Stothers [97] reported an association in males with LUTS between trends in NIRS parameters during dysfunctional voiding and a UDS diagnosis of bladder outlet obstruction (BOO). In a cohort of 70 subjects evaluated using UDS and simultaneous NIRS it was then identified that in those diagnosed with BOO the predominant NIRS pattern was a negative trend in tHb often associated with a fall in O$_2$Hb Figure 5 [98]. This negative trend implies a reduced or absent hemodynamic response and/or a reduction in the availability of oxygenated blood during detrusor contraction [40]. In contrast, most of those not classified as having BOO using the UDS diagnostic nomogram (Abrahams Griffiths) [99] had NIRS patterns of change similar to those seen in asymptomatic subjects, showing some degree of positive trend in tHb and/or O$_2$Hb (e.g. as in Figure 4).

NIRS data indicative of similar hemodynamic abnormalities are also seen in tissues other than the bladder. This occurs in muscle for example where there is an unmet increase in metabolic demand, and/or impairment of the normal response of the microcirculation [1,3,4,10,100-104]. Under these circumstances, the functional capacity of the muscle or organ is adversely affected, and during work involving contraction symptoms of dysfunction result. Hence the probable relationship between pathologies involving the bladder, lower urinary tract symptoms indicative of detrusor muscle dysfunction, and NIRS changes reflecting impaired hemodynamics and/or oxygenation.

The observed association of bladder outlet obstruction with specific trends in NIRS-derived hemodynamic parameters offered the potential for construct of a diagnostic algorithm. The initial version was compared to the UDS diagnostic nomogram for identifying BOO, and combined the trend in tHb/O$_2$Hb with two other non-invasive parameters, residual volume of urine post voiding (PVR) [99] and maximum urine flow rate (Qmax) [97]. Comparable diagnostic sensitivity and specificity was found between this initial non-invasive parameter algorithm (Sensitivity 85.71-89.3, Specificity 87.5-90) and the ‘gold standard’ invasive UDS nomogram [95]. This diagnostic ability was then confirmed in all but one [105] of five independent studies [98,105-108]. To date, the comparable discriminant ability of non-invasive parameters to invasive UDS criteria has been demonstrated for four separate algorithms [98,106-109], including one based solely on NIRS-derived data [109]. This latter algorithm was generated by classification and regression tree (CART) analysis of NIRS data collected simultaneously throughout voiding during UDS studies on 64 patients [109,110]. CART is a well-established and robust methodology for mathematical modelling of non-linear components [111,112]; examples of other diagnostic algorithms using CART include ones for early diagnosis of acute myocardial infarction in non-traumatic chest pain and classification of patients with unknown primary carcinoma [113,114]. The diagnostic ability of NIRS derived data incorporated in these algorithms strengthens the hypothesis that a disorder of detrusor hemodynamics is the principal physiologic anomaly underlying the voiding symptoms in patients with bladder outlet obstruction.

However, additional patterns of change are now evident in some males with BOO, including ones that have been identified in bladder dysfunction due to other pathologies. For example a negative trend in O$_2$Hb during voiding has been observed associated with an increase in the concentration of HHb, and/or a rise in tHb predominantly due to an increase in HHb, as illustrated in Figure 6. These changes imply that an imbalance in oxygen supply and demand occurs in the detrusor under these circumstances. Hence NIRS patterns of change in patients with BOO suggest that the pathophysiology underlying a patient’s symptoms can vary. While detrusor dysfunction resulting from an abnormal hemodynamic response during
voiding is the predominant finding, abnormalities in oxygen supply and demand can also occur as the detrusor contracts. Sometimes these physiologic events are associated; and on occasions the chromophore changes imply that ischemia develops in the detrusor.


Figure 6. A composite graph of UDS data with NIRS parameters in a 64 year old man with a 5 year history of increasing obstructive LUTS (difficulty initiating urination, a weak stream, and slow flow). As detrusor pressure (Pdet) increases prior to uroflow there is a decrease in O₂Hb reflected by a fall in tHb, and HHb begins to rise. During uroflow this positive trend in HHb increases, some rise in O₂Hb is evident following peak flow (Qmax), but the associated rise in tHb predominantly reflects a greater rise in HHb concentration. This implies an imbalance in oxygen supply and demand during voiding.

Detrusor overactivity and over active bladder. A number of investigators have now used NIRS to study subjects whose symptoms suggest over active bladder (OAB) and where detrusor overactivity (DO) is evident in UDS studies. However, both OAB and DO are recognized to occur due to a number of distinct causal etiologies which include: brain lesions, spinal cord pathology, microvascular disease, local bladder pathology, prostate, or lower urinary tract disease. While two studies do suggest NIRS as a relevant diagnostic tool for OAB [115,116], in our experience NIRS changes occurring in these patients are generally not synchronized significantly enough with episodes of DO (as defined by UDS study criteria), or consistent enough in their patterns of change for NIRS to be used for diagnosis [117]. However the relevance of NIRS in patients with DO and OAB is that published and unpublished data from simultaneous monitoring during UDS have documented several distinctive chromophore patterns associated with episodes of bladder overactivity and the principal symptom of concern, involuntary leakage of urine.

These patterns of change in OAB/DO suggest that each of the following physiologic events probably predispose patients with OAB/DO to episodes of involuntary urinary leakage:
• normal (albeit involuntary and untimely) bladder contraction that is likely neurologically mediated,
• a fall in blood volume indicative of a dysfunctional hemodynamic response in the detrusor microcirculation,
• oxygen debt/hypoxia; with NIRS changes that in voluntary muscle are associated with fatigue during contraction, and
• the onset of detrusor ischemia in rare instances.

It is significant that each of these patterns is comparable to NIRS data obtained in other tissues which reflects monitoring of specific physiologic events: hence the NIRS bladder findings support there being multiple underlying causal mechanisms for these patients’ symptoms. This in turn supports the belief that a single NIRS pattern of change would be not be a robust diagnostic measure in DO nor OAB, but that simultaneous NIRS monitoring during UDS evaluation of these patients could add data related to detrusor hemodynamics and/or oxygenation of relevance to understanding why a patient’s symptoms are occurring. From this additional information choice from the therapies available could be made to specifically match the physiologic and/or functional basis of their symptoms.

Non-neurogenic lower urinary tract dysfunction. Five asymptomatic children (5-7 years) were studied during natural voiding using the ‘Portamon’ wireless device and software [34] and their data compared to a group of 16 symptomatic children (5-17 years) with non-neurogenic voiding dysfunction (NLUTD) [118,119]. All the subjects were monitored successfully and the children liked the device which they compared to a small cell phone.

In all asymptomatic children the pattern of change in chromophore concentration was comparable and matched adult patterns, although the magnitude of change and duration of voiding varied between individuals. Figure 7 illustrates 4 graphs of representative patterns for asymptomatic children; all asymptomatic subjects showed 3 consistent elements during the 3 phases of voiding analyzed:

• a brief initial increase in \( O_2Hb \) and \( tHb \) on permission to void;
• a greater and longer sustained increase following the start of uroflow;
• a strong positive trend in \( O_2Hb \), with minimal or no change in HHb, throughout, or for the majority of the voiding cycle.

In these children, as in asymptomatic adults, the data indicate that an increase in \( O_2Hb \) occurs with a resultant rise in blood volume in the detrusor, which in the context of the microcirculation [61-63] reflects full provision for the metabolic requirements of normal muscle function, although, as happens in healthy voluntary muscle, the increase in \( O_2Hb \) exceeds actual oxygen demand [3,10]. Conversely, in children with NLUTD the patterns of change were markedly different. Four examples of the commonest chromophore pattern during voiding are shown in Figure 8. All symptomatic children had a predominantly negative trend in \( O_2Hb \) and \( tHb \) in contrast to the positive trend seen in asymptomatic children. The NIRS elements seen during the 3 phases of voiding were:

• little or no increase in \( O_2Hb \) following permission to void, with the majority of children having a downward trend;
• a further fall in \( O_2Hb \) and \( tHb \) usually followed the start of urine flow;
• for the remainder of voiding a negative trend in $O_2$Hb occurred (often with periods of major decrease, although temporary, intermittent or fluctuating rises, or a delayed increase were also observed), and overall the changes in $O_2$Hb were greater than for HHb which remained at a higher concentration.

The predominant pattern in this group of no initial increase in $O_2$Hb on initiation of voiding, and a decrease in $O_2$Hb and tHb during bladder contraction (urine flow), implies physiologically a blunting or lack of the hemodynamic response required to provide energy for detrusor contraction, and the potential for fatigue (exercise intolerance), as happens in striated muscle [10,104,120].

Figure 7. Examples of NIRS voiding data sets from 4 asymptomatic children (A 12 yrs, B 5 yrs, C 13 yrs, D 15 yrs). A positive trend in $O_2$Hb and tHb is evident which begins on permission to void and continues for all or the majority of uroflow, while HHb remains essentially unaltered.

Figure 8. Examples of NIRS data sets from 4 symptomatic children with dysfunctional voiding due to NLUTD. All show a negative trend in $O_2$Hb and tHb from permission to void (P) that continues through uroflow start (S), and a fall in $O_2$Hb and tHb during a substantial portion of the voiding cycle, while HHb concentration remains higher and shows lesser degrees of change.
In the children whose voiding dysfunction was associated with symptoms of weak urinary stream and fluctuant urine flow hemodynamic change was often evident which implied that detrusor blood volume rose and fell intermittently during voiding. This is illustrated in Figure 9.


Figure 9. Simultaneous data (uroflow, EMG, voided volume, and NIRS pattern of chromophore change) in a child with non-neuropathic lower urinary tract dysfunction. Following permission to void (P) an increase tHb occurs due to an equal increase in O$_2$Hb and HHb, then a sharp decrease in tHb is evident predominantly due to a fall in O$_2$Hb that continues as uroflow starts (S), fluctuations in tHb/O$_2$Hb follow, but the hemodynamic trend is negative from 23 seconds to the end of urine flow (E), while HHb remains stable. This pattern implies hemodynamic fluctuation during voiding with variations in the availability of O$_2$Hb and total blood volume in the detrusor.

In one subject who had a urethral stricture and these same symptoms (weak urinary stream and fluctuant flow), hemodynamic variations during voiding were followed by a rise in HHb and a fall in O$_2$Hb towards the end of uroflow, implying the onset late in voiding of an imbalance in oxygen supply and demand (oxygen debt). Figure 10.

And in 3 of the 17 symptomatic children with NLUTD this same pattern of change began abruptly on initiation of voiding and continued throughout their efforts to void. Figure 11 is a representative example of this pattern with the relationship to uroflow and voided volume illustrated. O$_2$Hb can be seen to decline steeply on permission to void with an opposite and almost equal increase in HHb, while tHb remains essentially unchanged, and this overall chromophore trend continues throughout voiding. These children had severe symptoms. This
‘equal and opposite’ pattern of change in O$_2$Hb/HHb in the presence of a stable tHb matches the characteristic NIRS pattern observed in muscle [4,6,100] and the rabbit bladder [121] in response to hypoxia (see Figure 15 in Animal Experiments).


Figure 10. Voiding chromophore data (overlaid and biased to zero at permission to void) in a boy with voiding difficulty due to a urethral stricture (weak flow and fluctuant urinary stream). Fluctuations in O$_2$Hb/tHb are evident during voiding, and just prior to peak flow (Q) a progressive rise in HHb begins that continues through the end of uroflow and at 60 seconds is associated with a fall in O$_2$Hb, while tHb remains stable. This implies hemodynamic variations in the detrusor, and the onset of oxygen debt during the later stages of voiding.


Figure 11. Data from a simultaneous UDS and NIRS study in a child with severe voiding difficulty due to NLUTD. NIRS data are overlaid and biased to zero at permission to void (P) where a sharp decrease in O$_2$Hb is evident with a coincident equal and opposite increase in HHb, while tHb remains stable. Between uroflow start (S) and uroflow end (E) O$_2$Hb shows an overall downward trend while HHb rises further initially and then plateaus; tHb rises briefly and then falls reflecting simultaneous changes in O$_2$Hb and HHb. The overall chromophore pattern implies initial ‘oxygen debt’, and an imbalance of oxygen supply and demand and the potential for muscle fatigue during voiding.
As children with NLUTD have no known anatomical or neurological basis for their symptoms [34] it is probable that the physiological basis for their voiding dysfunction is disordered detrusor hemodynamics and oxygen delivery.

*Neurogenic bladder.* One of the most important conditions where there is loss of normal bladder function is spinal cord injury (SCI). It is estimated that 86,500 patients with SCI currently live in Canada, and that approximately 4,300 patients are newly diagnosed with SCI annually [39]. One of the commonest and most serious consequences of SCI is loss of normal bladder function; this occurs in more than 80% of patients and predisposes them to a wide range of acute and chronic urinary tract complications that adversely affect their health-related quality of life [122]. However, currently, evaluation of bladder function is limited to periodic invasive urodynamic testing. Effective non-invasive optical monitoring would provide the option for patients with SCI to have more frequent assessments than are possible with an invasive procedure, and wireless systems have the potential to be used for long term evaluation; even home based monitoring could be contemplated with cell phone transfer of data for review by urologists.

![Figure 12](image)

Figure 12. A composite graph of simultaneous UDS and wireless NIRS data in a paraplegic patient with a neurogenic bladder. An upward trend in $O_2$Hb and $t$Hb is evident as the bladder fills with an abrupt decrease occurring during two episodes of detrusor over activity with urge incontinence and urinary leakage (L). Prior to each urinary leak there is an associated fall in TSI % as detrusor pressure ($P\text{ det}$) rises.
A pilot study in 10 subjects with SCI (age range 18 – 75 years) [39] combined wireless NIRS monitoring with conventional UDS testing. Changes in O$_2$Hb, HHb and tHb, and tissue saturation index (TSI %) were monitored, time points for symptoms of urgency and urinary leakage were recorded, and patterns of change in NIRS parameters compared to standard urodynamic pressure tracings. The data showed strong consistency between changes in NIRS-derived tHb and changes in intravesical pressure during filling across subjects. Bladder filling was associated with a gradual increase in O$_2$Hb and tHb with minimal changes in HHb. Further studies are required to confirm these qualitative findings and measure them quantitatively. In addition, a drop in TSI% was identified to occur seconds before urinary leakage. Figure 12. This finding offers the potential for a monitoring system to be developed to warn patients of impending involuntary leakage. They could then electively use their regular routine for manually expressing or draining their bladder, and by avoiding incontinence could improve their quality of life.

Interstitial cystitis. Shadgan et al [123] reported the potential of spatially resolved (SR) NIRS as a means of identifying interstitial cystitis ‘Painful bladder syndrome’ (IC/PBS), a symptom complex of urinary urgency, daytime frequency, and suprapubic pain/pressure/discomfort, in the absence of a positive urine culture or another obvious bladder pathology [124]. To date no definitive causal etiology or definitive diagnostic methodology has been identified for IC/PBS, and diagnosis is currently based on clinical judgment after ruling out other urinary pathologies through physical examination, laboratory tests, cystoscopy, and invasive urodynamic studies (UDS). As one potential etiology is inflammation of the bladder mucosa associated with abnormal angiogenesis and ulcerative lesions, SR NIRS was explored as an evaluation measure, as such inflammatory changes are known to be associated with an alteration in hemodynamics and oxygenation in other tissues [125]. In a pilot study of 4 female subjects with IC/PBS resting detrusor oxygen saturation (TSI %) was found to be significantly higher than in 20 control patients with lower urinary tract symptoms due to other bladder conditions (P<0.0005, TSI % mean 74.2% ±4.9 vs. 63.6% ±5.5) [122]. This observation supports the literature reporting inflammation of the bladder mucosa as a significant etiology in patients with PBS/IC [123,124]; demonstrates the feasibility of monitoring SR NIRS-derived bladder wall TSI% in this patient group; and indicates the potential of using resting TSI % as a physiologic evaluation measure for PBS/IC. With further studies this technique may offer a non-invasive diagnostic option in this condition, or a screening measure for monitoring the evolution and response to treatment.

Functional NIRS of the Bladder

Macnab et al. have reported the use of a 5 X 5 cm two channel four point NIRS array to transcutaneously map dynamic change of detrusor hemodynamics during voiding [126]. The array uses the established principles of functional near-infrared spectroscopy (fNIRS) developed for brain mapping, where multi-channel instruments with grids of source-detector pairs are used to detect regional change in oxygenation/hemodynamics [28,127]. The array was placed on the abdomen over the bladder of an asymptomatic adult male. In 4 separate trials, after natural bladder filling NIRS-derived changes in oxyhemoglobin O$_2$Hb, deoxyhemoglobin HHb and total hemoglobin tHb concentration were recorded during voiding (measured via uroflow), using 4 channels of a 4 wavelength instrument (‘Oxymon’ Artinis
Medical Systems, BV, The Netherlands). Video images were generated using incorporated topographic mapping software. This series of fNIRS bladder studies generated reproducible chromophore data consistent with single channel monitoring during natural voiding, but the dynamic color video and larger tissue area monitored potentially offer new methodology for investigating regional variations in bladder oxygenation and hemodynamics. Changes in tHb occurred following permission to void that predominantly reflected variation in O$_2$Hb; tHb peaked at maximum urine flow then fell to a nadir lasting to uroflow end, and the changes in fNIRS video color intensity correlated with graphic change in chromophore concentration. (This video can be viewed at http://link.aip.org/mm/JBOPFO/1.3122886/072902jbov1.mov). The fNIRS video appears to confirm what is known about the unique coiling/uncoiling mechanism of the bladder vasculature, that accommodates for changes in thickness of the bladder wall as the organ alters in size as it fills and empties [42,45], as the waves of color variation observed in real time across the mapped area suggest regional hemodynamic variation.

**Monitoring Sphincter and Pelvic Floor Function**

A transvaginal NIRS probe developed by Shadgan et al. [128] can be used to interrogate the urethral sphincter and the muscles of the pelvic floor. Development of the probe utilized miniature sensors (3 x 8 x 14 mm) and optical cables (diameter 2.0 mm). The tips of each of the two miniature cables were connected to the standard fiber-optic cables of a commercial NIRS instrument via a custom made plastic block interface with screw threaded holders; the Oxymon III (Artinis Medical Systems, BV, The Netherlands) had wavelengths of 764, 855, 904 and 975 nm and its regular commercial software [26]. The paired NIRS detectors were configured so that with the probe in position they would appose the bladder detrusor and mid-urethra respectively through the anterior vaginal wall. The emitter was placed mid-way between the detectors which were positioned 1 and 5 cm from the tip of the probe. This configuration provided good sampling sensitivity and an interoptode distance of 2 cm. The emitter/detector array was laid on high density plastic foam shaped to provide a snug push fit when inserted into the probe housing; a disposable vaginal speculum made of transparent plastic.

Reproducible tracings (change in O$_2$Hb, HHb and tHb) were achieved during spontaneous voiding in all trials attempted (8 separate probe insertions in a healthy 67-year-old female volunteer). Events monitored during each trial also included coughing, Valsalva maneuver, and a series of voluntary pelvic floor contractions. Each event had a characteristic pattern of change, and during sequential pelvic floor contractions there was good reproducibility of the patterns and magnitude of change generated in the channel monitoring over the mid-urethra, and an absence of significant movement artifact [128]. An example of one such series of four pelvic floor contractions is shown in Figure 13.

Two parameters derived from such NIRS data are of potential interest in pelvic floor muscle (PFM) training; the recovery interval of muscle oxygenation and the muscle reoxygenation rate. Kegel exercises are the central component of many regimens for restoring pelvic floor function after childbirth, and address symptoms of involuntary urinary leakage (stress incontinence) which occur. However, the optimal exercise program is elusive as objective measures of improvement in muscle function are lacking [129]. Pilot data indicate
the potential of NIRS measurements during voluntary PFM contraction to provide two quantitative measures based on comparison of the slope of recovery after pelvic floor contraction (see overlay on Figure 13) [130]. The recovery interval of muscle oxygenation is the time needed for the recovery of O$_2$Hb concentration from the maximum level of deoxygenation at the end of contraction to the maximum level of reoxygenation during the post-activity rest period. The recovery interval reflects the influx of oxygenated arterial blood and continued oxygen utilization during recovery [100,131]. The muscle reoxygenation rate is calculated as the rate of increase in O$_2$Hb during the initial 3 seconds immediately after cessation of exercise. This reflects the velocity at which recovery starts after exercise and is directly related to muscle microvascular function. These measurement parameters could allow physicians to individually assess patients and quantify the efficacy of PFM training regimens pre and post intervention by monitoring changes in pelvic floor oxygenation, using the minimally invasive NIRS assessment technique described [128].

![Figure 13](image.png)

**Figure 13.** Chromophore data collected transvaginally showing 4 consecutive sustained pelvic floor contractions. Overlaid are the points used to quantitate recovery from contraction using the recovery interval of muscle oxygenation, and muscle reoxygenation rate.

**Effect of Pharmacological Agents**

Cohorts in therapeutic trial evaluation of alpha blocking agents have also been studied; these are vasoactive drugs of growing relevance in the treatment of voiding dysfunction [132]. We have also seen patterns of chromophore change consistent with those in asymptomatic subjects in a child with a history of non-neurogenic lower urinary tract dysfunction following treatment with alpha blockers. NIRS parameters may well be of value in the evaluation of the effects on the bladder of other pharmaceutical agents currently becoming available for treatment of voiding dysfunction.
THE RELEVANCE OF NIRS IN UROLOGY

NIRS monitoring is able to provide a range of data that reflect physiologic change occurring in tissues within the genitourinary tract. In particular NIRS bladder monitoring now contributes novel physiologic information on changes in detrusor hemodynamics and oxygenation as the bladder fills and empties that add knowledge regarding normal bladder physiology and are relevant in the context of voiding dysfunction [12]. Although the body of literature on bladder NIRS is still small it is clear that it is already possible to identify distinctive patterns of change in chromophore concentration in a range of conditions causing voiding dysfunction. Hence, as experience with non-invasive optical monitoring of the bladder grows it is probable that distinction will be possible between a larger number of specific bladder pathologies based on the nature of the physiologic changes in oxygenation and hemodynamics evident in each condition. The information that NIRS monitoring can provide is relevant for more comprehensive diagnosis of the underlying cause of bladder problems, and closer matching of therapy from the medications available to the causal mechanism of the symptoms by basing selection on the site and mode of action of the drug. And, as further studies occur urologists will identify where and in what conditions NIRS is best utilized. Conducting UDS pressure flow studies with simultaneous bladder NIRS has obvious relevance, and validation of diagnostic algorithms based on chromophore patterns of change may provide a new screening methodology, or non-invasive diagnostic approach to bladder dysfunction, of relevance in some contexts.

Other previously reported NIRS applications in urology contributed significantly to the evolution and relevance of this technology for bladder studies and many of the concepts explored still have relevance [11,25]. The ability to measure hemodynamic changes in the testis remains relevant, and NIRS is a legitimate means of study [76]. Development of less toxic contrast media has long been a subject of research in uroradiology [84]. Contrast agents have a direct effect on glomerular filtration and medullary blood flow, but now addition of a prostacyclin analog can prevent the negative effects of contrast on the microcirculation. The measurement of renal tissue oxygenation by NIRS is probably a useful adjunct to such research; successful animal studies support this, although the depth of penetration of NIR light limits non-invasive application in adult human subjects. The maximum depth of NIR photon penetration is reported to be 6 cm [1] but the effective depth for monitoring is less. However, renal studies can be done successfully in neonates [82], and probably are feasible in children. There are obvious advantages to using NIRS to study renal blood flow, including its non-invasive nature and non-toxic energy source, the ability to study patients at the bedside, and the ability to continuously collect data over time.

NIRS has been used extensively to study human muscle metabolism and these studies are based on validated principles. In children with end stage renal disease oxidative metabolism is impaired in skeletal muscle during exercise, and metabolism improves remarkably after renal transplantation. NIRS is recommended as a useful method to monitor muscle metabolism in such children.

While penile NIRS offers non-invasive evaluation of vasculogenic erectile dysfunction, the role of NIRS as a diagnostic entity in this condition remains unclear; the reality is that the wide availability and acceptance of therapies to improve erectile dysfunction using
pharmacologic agents probably make NIRS-related and other diagnostic entities largely redundant.

**Wireless NIRS**

The ease of use of CW NIRS wireless devices and the reproducibility of the data obtained with the ‘Portamon’ by our group and others confirm the feasibility of using miniaturized, portable NIRS technology with telemetric capacity for human clinical studies [11,16,30,34]. Such devices are already expanding the scope of biomedical applications of NIR spectroscopy, as evidenced by the growing body of data on oxygenation changes in skeletal muscle and the brain, and applications in other clinical areas such as urology, neurosurgery and orthopedics.

Several wireless SR NIRS devices have received USA Food and Drug Administration approval, although many investigators have concerns that technical limitations currently compromise the applicability of tissue oxygen saturation measurement, particularly involving the brain [6]. Wolf et al [133] have reviewed the use of NIRS in newborns; and these devices have been shown to demonstrate changes that correlate with alteration of important physiologic variables. But there are several key differences between the available instruments and the algorithms they employ, and hence the data generated does differ between instruments. In the context of muscle physiology studies SR NIRS technology is more widely accepted as a means of measuring absolute values for muscle oxygenation; and this parameter is viewed as valuable, as it allows quantitative comparison to be made among exercising muscles and between different subjects [16]. And in urology TSI % promises to be a valuable additional component for evaluating bladder function. It is likely that as wireless device technology evolves further and algorithms related to SR spectroscopy continue to be refined that the reliability and reproducibility of brain and muscle measurements will advance, and future studies will identify improved performance and validity. Conceivably wireless devices could also be developed to address a number of clinical scenarios where the feasibility of conventional NIRS measurement has already been demonstrated, as they have for NIRS bladder monitoring. Examples include detection of the onset of ischemia in the spinal cord in real time during surgery; monitoring of perfusion in cases of tourniquet-induced limb muscle ischemia; and non-invasive measurement of tissue pH and glucose [6,133,134].

In the future, inexpensive devices could be developed for use on a large scale, and software applications developed to transmit NIRS data to a care giver or researcher using a mobile phone. A prototype wireless NIRS device has been trialed that incorporates a 975 nm NIR light source [135]. As water has an absorption peak at 975nm this device can be used to detect water content in the bladder and differentiate between an empty bladder, one with low volume, and a full bladder. This will enable detection of when the bladder has filled to a defined volume, which is a relevant measure for those with neurogenic bladder as both a quality of life measure by allowing voluntary emptying before accidental incontinence, and as a protective entity where a risk of renal damage due to back pressure exists. This device could also be explored in the context of managing enuresis in children and loss of continence in the elderly. A variety of wireless NIRS devices have the potential to be employed in areas of the world where medical resources are scarce, as in these environments monitoring bladder...
function coupled with the use of appropriate diagnostic algorithms could offer screening tests able to identify those requiring access to limited specialized medical services.

Confidence and Reproducibility of Bladder NIRS

The reasons for confidence that NIRS monitors the detrusor muscle in the anterior bladder wall and that the data obtained reflect physiologic change have been reviewed [11,25,30,34,40]. As described in this chapter the basic physics principles of NIR light transmission lend themselves to study of the bladder, as do the vasculature and contractile properties of the organ.

These properties are integral to the way the bladder fills and empties and are impacted by disease. And confidence in the information bladder NIRS provides can be drawn from NIRS-inferred physiologic changes evident in studies in other tissues matching those seen in the bladder, and the fact that the patterns of change occurring in specific forms of voiding dysfunction are seen consistently.

The principal way of altering the depth of the path of NIR light through tissue is to alter the interoptode distance (IOD), the distance between the NIRS emitter and detector. The point of maximum sensitivity is usually at a depth that approximates half the IOD, although the photon path extends above and below this point. Thus selecting an appropriate IOD enables the photon path to be directed to interrogate the detrusor in the anterior bladder wall.[11,24,30]

With the 4 cm IOD usually used for bladder NIRS, light attenuation will take place within the anterior wall of the bladder, with NIR photons travelling through the skin and subcutaneous tissue making the contribution of these structures minimal. The ability of photons to penetrate in this way is supported by brain studies addressing a comparable issue; namely the ability to interrogate the cortical surface of the brain reliably in spite of photons having to travel through skin, muscle, bone and cerebrospinal fluid to reach the tissue of interest.[6,136]. Also by the advent of SR spectroscopy where with our current wireless device [30,33] bladder NIRS data can be analyzed at three slightly different depths of penetration; although the differences in data collected are small, they clearly indicate that attenuation of NIR light does differ related to interoptode distance. Figure 14.

Animal experiments using an accepted urologic model also provide an additional measure of confidence[121].

Similar patterns of chromophore change were observed in the rabbit bladder during filling to those that occur in humans, and comparable changes were recorded during hypoxia to those observed in muscle. Changes during three consecutive cycles of induced hypoxia (Sao2 decreased to 80% via rebreathing circuit) were highly reproducible, both when NIRS monitoring was done transcutaneously and when optodes were placed directly on the wall of the surgically exposed bladder Figure 15; (i.e. with and without subcutaneous tissue between the optodes and the bladder). An appropriate IOD was used in each circumstance to account for the different depth of light penetration required. As a terminal intervention the organ’s blood supply was then clamped, and changes in O2Hb and HHb concentration indicative of ischemia occurred immediately.
Figure 14. Data from bladder monitoring in a child using a spatially resolved (SR) NIRS device, showing an example of the difference in chromophore patterns when data are analyzed at each of the three depths of penetration (DOP#s approximately 20, 17.5 and 15 mm) achieved by having three different emitter to detector (interoptode) distances.

Figure 15. NIRS data collected from the surface of a surgically exposed bladder in a rabbit model during three cycles of induced hypoxia. A consistent and reproducible pattern of chromophore change is observed that matches the generation of hypoxia in voluntary muscle and other tissues.

In human studies, significant variations in NIRS parameters only occur in direct temporal relationship to events in the voiding cycle, and patterns compatible with physiologic change are only detected over the bladder - not from a control channel with the same IOD sited elsewhere on the abdomen. Also, comparing NIRS bladder data with those from muscle,
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brain, and other tissues indicates that reproducible and recognizable physiologic effects occur in the microcirculation due to specific systemic and organ pathology [2,10,6,34,43,100-102,103,104,137]. Systemic pathologies affecting the vasculature of the human body also compromise the ability of the detrusor microcirculation to respond adequately to an increase in oxygen demand during contraction. And local bladder pathology such as bladder outlet obstruction generates organ-specific changes in the detrusor muscle that adversely affect blood flow, muscle metabolism, and contractility.

An obvious concern is what effect movement may have on the collection of NIRS bladder data. An important improvement in this regard is the rigid mounting of the emitter/detector components of our wireless device, as any movement that changes the interoptode spacing to any degree during NIRS measurement alters the photon path length and invalidates the data. This could sometimes be a problem with early iterations of adhesive patch interfaces for laser powered devices. Wireless device specifications can also include an accelerometer to overcome distortion from motion artifacts; the effects of motion on NIRS data can also be tempered using active noise control [138] and wavelet transformation has been used to remove artifact caused by repositioning limbs being monitored during orthopedic surgery [139], although we have not evaluated these approaches in bladder studies.

In practice, during bladder monitoring any spontaneous movement by the patient is readily evident in the NIRS data stream as an abrupt unidirectional change of short duration in the magnitude of all three parameters (O$_2$Hb HHb and tHb); a pattern of change incompatible with a physiologic effect. Importantly these abrupt effects do not usually compromise the ability of physiologic trends in the data to be identified, contrary to reports from some investigators new to NIRS studies. Such data should not be discarded, although occasionally if movement episodes are prolonged or extreme baseline shifts occur which can be problematic. When abdominal contraction occurs during voiding effort, and the required electrodes and catheters are in situ during UDS studies, a simultaneous change in all NIRS parameters again occurs in conjunction with increased electromyogram activity and a significant rise in abdominal pressure (measured continuously via rectal catheter). Small magnitude fluctuations in the NIRS graphic display are routinely seen that correspond to respiratory movement and/or vascular pulsation [16]; these are identifiable as they are rhythmic, regular and of low amplitude, and do not compromise data collection or interpretation. Conventional data filters and where necessary custom software algorithms can be used to smooth data and remove motion artefact retrospectively, or via incorporation into a NIRS instrument’s software.

Importantly is should be recognized that one of the proven attributes of NIRS is the ability to generate meaningful data in the presence of movement. Evidence that this can be done effectively comes from exercise physiology research and muscle studies done in a laboratory setting, and during a variety of sporting activities e.g. running, skiing, and wrestling, and in other voluntary activities where significant movement occurs [11].

Another legitimate question is do the changes in bladder size that occur as the organ fills and empties impact on the validity of NIRS measurements? As reported, the anatomy of the bladder and ultrasound evidence of how its dimensions alter during phases of the voiding cycle provide confidence that meaningful monitoring can be achieved, as the relationship of the anterior wall of the bladder to the abdominal sensor remains relatively constant during voiding. The site chosen for the NIRS sensor patch 2 cm above the pubis and across the
midline also appears to be optimal; ultrasound studies suggesting that in this location there is least change in the relationship between the anterior abdominal wall and the skin surface [41].

Two other observations also support NIRS bladder data providing information that is uncontaminated by alterations in the organ’s size or position. Between the conscious decision to void and the start of urine flowing there is evidence of significant hemodynamic change occurring from the increase in tHb/O_{2}Hb that occurs. And as this change is seen before voiding begins it occurs while the bladder volume remains constant and no change in bladder size has occurred, and thus in all probability represents physiologic change. NIRS patterns of change indicative of alterations in detrusor oxygenation and hemodynamics have also been observed where there is voiding delay due to a common condition known as ‘shy’ bladder [30]. Significant variations in the concentration and trends of O_{2}Hb, HHb and tHb have been documented in such cases that are individually indicative of changes in blood volume, an increase in the availability of oxygen, and increases in oxygen consumption, where the bladder volume remains constant as no urine is passed. An example is shown in Figure 16. Such changes most likely represent the effects of isovolumetric contraction of the bladder during a sustained urge to void, and the resulting effects on the detrusor microcirculation. Consequently it is more probable than not that that change in bladder size does not negatively impact the ability of NIRS to provide monitoring data of value during evaluation of patients with voiding dysfunction.

The diagnostic ability of the algorithms based on NIRS derived data supports the hypothesis that a disorder of detrusor hemodynamics is the physiologic anomaly underlying the voiding symptoms in patients with bladder outlet obstruction. The first algorithm iteration, that combined NIRS trend data with two other non-invasive parameters, had comparable discriminant ability to invasive pressure flow studies in terms of classifying symptomatic males as having an obstructed or unobstructed bladder [98]. And then NIRS data used alone proved equally discriminant in a classification and regression tree (CART) algorithm [109,110]. Importantly, other investigators reported comparable results using both the initial combined data algorithm [106], and two others that were similar but independently derived [107,108]. Diagnostic discriminant ability with this degree of reproducibility would be unlikely if change in bladder size or other artefact contributed to any meaningful degree to bladder NIRS data.

Non-invasive NIRS monitoring of bladder hemodynamics and oxygenation during voiding, including absolute measurement of tissue saturation (TSI %), is now recognized to contribute novel physiologic information unavailable by other means [12]. TSI % in particular has importance as a monitoring entity as it is an absolute measure of tissue oxygenation, and hence comparison can be made in the same individual to assess alterations in this parameter indicative of inflammatory changes in the bladder mucosa such as occur with interstitial cystitis, or impairment of oxygenation in a testis rendered ischemic due to torsion. Comparison of absolute tissue oxygenation measurements between the right and left testes using NIRS has recently been shown to allow testicular torsion to be reliably identified, indicating the ability of real time NIRS-derived data to be used in the assessment of this important acute urological condition [76].

Importantly there is also consistency and reproducibility in the patterns of change in O_{2}Hb and HHb concentration from baseline observed in bladder NIRS studies, and between these data and physiologic events monitored using conventional NIRS in other tissues.

Figure 16. Changes in chromophore concentration in an asymptomatic adult experiencing voiding delay. Spontaneous movements by the subject at 19 and 98 seconds [bold arrows] displaced the data, hence, data points for these periods were removed [horizontal line] for clarity of chromophore trends. A period of 138 seconds elapsed where no urine was passed and hence bladder size and position were unaltered. But, between permission to void and the start of uroflow changes in blood volume (tHb) and O2Hb are evident indicating hemodynamic change, and the trend of increasing HHb indicates rising oxygen consumption. Uroflow finally starts after marked hemodynamic change; a sustained increase in tHb/O2Hb, and an abrupt fall in HHb that follows.

This body of work is relevant to bladder monitoring as it provides comprehensive NIRS data on the effects of a variety of specific physiologic events and the similarity of these changes in different tissues. Such events include changes in blood volume, ischemia, variations in oxygen supply and demand, hypoxia, the effect of fatigue, and the impact of disease and aging. While the body of NIRS bladder research is small in comparison, it is evident that comparable and reproducible effects occur in the bladder in response to many of these same physiologic events, and in the presence of symptomatic bladder dysfunction. Consequently reference to the broader literature assists in the interpretation of NIRS applications in urology; and with bladder NIRS data in particular can enhance the investigation of patients with symptoms of voiding dysfunction, and also contribute to a greater understanding of normal bladder physiology and the etiology of lower urinary tract pathology.

In addition to the information NIRS bladder monitoring provides, this optical technology is attractive in the context of evaluation of voiding dysfunction because of its non-invasive nature, ready acceptance by patients, and ability to be used in conjunction with existing evaluative modalities. Wireless devices now have several advantages over conventional laser powered NIRS instruments, and expand the potential for urologic applications of NIRS by offering new monitoring options; they also have obvious relevance in other clinical studies and fields of research.

There is also the potential following further studies by urologists for NIRS to be used alone as a screening tool, for monitoring tissue oxygenation changes or bladder filling, or as a
diagnostic entity, although there is resistance to diagnostic application due to a perceived lack at present of effective diagnostic devices incorporating NIRS. However, even if NIRS were only to be used in conjunction with simultaneous conventional UDS pressure flow monitoring studies the additional physiologic information available to clinicians should contribute to better understanding of causal pathology in patients with voiding dysfunction, aid logical choice of therapeutic agents, and provide a measure of treatment efficacy.

Whether NIRS comes to be used in urology for research, clinical study, or diagnosis is for basic scientists and urologists to determine through further collaborative studies. However, from the research done to date there are strong grounds to undertake the due diligence required to establish where NIRS can and cannot contribute. In urology, as in other fields and applications, it is of particular importance in this process to use lessons learned and knowledge acquired from NIRS studies in other tissues. The physiologic insights learned through NIRS research into muscle and brain function, the contributions of NIRS in exercise science, and the established clinical relevance of the scientific principles of NIRS in oximetry are key examples of why such knowledge should be translated across disciplines, and confidence drawn to explore clinical diagnostic opportunities. NIRS is often spoken of in the context of ‘having potential’; but in urology now represents a disruptive technology that can add to diagnostic evaluation and hence potentially benefit a significant population if appropriate studies are undertaken and the relevant clinical experience sought using this technology.

REFERENCES


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